## REMARKS

Claims 1, 6, 8, 18 and 32-55 are under examination in the present action. Claims 1, 6, 8, 18 and 32-55 are rejected.

Applicants respectfully request entry of the above amendments and reconsideration of the application in view of the above amendments and the following remarks.

No new matter is being added by the above amendments, nor are the claims altered in a manner that will require any additional search by the Examiner. The foregoing amendments are submitted without conceding the correctness of any rejection or argument put forth by the Examiner in the Instant Office Action or in any preceding Office Action. Rather the foregoing amendments are submitted solely to place the application in a better condition for allowance. Also, the foregoing amendments are submitted without waiver or prejudice to Applicants' right to pursue any subject matter canceled thereby in any continuing application, yet to be filed.

Rejections under 35 USC §112, 2d Paragraph

In the Instant Office Action the Examiner has rejected claims 6, 8, 18, 37, 43, 49 and 55 under 35 USC §112, 2d Paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as his invention. Applicants respectfully traverse this rejection.

Applicants have cancelled claims 6, 8, and 18 by the amendments submitted herewith. Accordingly, the rejection of claims 6, 8, and 18 under 35 USC §112, 2d paragraph, is obviated, and Applicants respectfully request withdrawal thereof.

Regarding claims 37, 43, 49 and 55, the Examiner has alleged that these claims "[a]re indefinite and confusing in the recitation 'Tyr(I)' because the expression is not defined in the specification or in the claim. Appropriate clarification is required." (Instant Office Action at page 3, last paragraph.)

The term "Tyr(I)" is an art-recognized term which is understood to connote an iodinated tyrosine residue. Iodinated tyrosine has been readily available to peptide chemists for quite a number of years - indeed iodinated tyrosine comprising radioactive

iodine has long been utilized in radioassay techniques. For the Examiner's convenience Applicants have submitted with the Information Disclosure Statement filed herewith a copy of European Patent Application No. 0 389 180 A1, (EP '180), which published on September 26, 1990, and United States Patent No. 5,708,135 (US '135), which issued on January 13, 1998. Applicants note that EP '180 is listed in the Instant Application among the references which are specifically incorporated by reference, (Instant Application at page 11, line 20), while US '135 first discloses the compound referred to in the Instant Application as BIM-23313. (Compare BIM-23313, which appears in the Instant Application at *inter alia*, page 12, line 9, to the compound appearing in US '135 at, *inter alia*, claim 8, line 48.)

The Examiner will note that the term "Tyr(I)" appears a number of times throughout each of these documents, and in each case the term refers to iodinated tyrosine. (In EP '180 see, *inter alia*, the peptide structure depicted in the abstract; lines 5-6 of the abstract; page 2, lines 22-23 and 32-41; page 3 lines 9-24 and 36-38; page 4, lines 6-45, and page 5, claims 1 - 6.) (In US '135 see, *inter alia*, column 2, lines 39-42 and 62-66; column 3, lines 1, 14 - 16 and 49 - 52.)

Applicants respectfully submit that the foregoing demonstrates that a person of skill in the art would immediately appreciate the term "Tyr(I)" to refer to iodinated tyrosine. Accordingly, the rejection of claims 37, 43, 49 and 55 under 35 USC §112, 2d paragraph, is obviated, and Applicants respectfully request withdrawal thereof.

Rejections under 35 USC §102(b)

In the Instant Office Action the Examiner has rejected claims 1, 6, 8, 18, 32-33 and 38-39, 44-45 and 50-51 under 35 USC 102(b) as being anticipated by Moller et al. (Clin. Science, vol. 75, pp. 345-350, 1998). Applicants respectfully traverse this rejection, both as put forth in the Instant Office Action at page 4 and at pages 7 - 11.

Applicants have cancelled claims 6, 8, 18, 33, 39, 45, and 51 by the amendments submitted herewith. Accordingly, the rejection of claims 6, 8, and 18 under 35 USC 102(b) as being anticipated by Moller et al., is obviated, and Applicants respectfully request withdrawal thereof.

Regarding claims 32, 38, 44 and 50, the Examiner alleges that Moller et al. disclose the use of a mixed SSTR-2/SSTR-5 agonist (SMS 201-995 or somatostatin-14) for the method of treating hyperlipidemia, for the reasons listed in the Instant Office Action at page 4 and at pages 7 - 11.

Without conceding the correctness of the Examiner's characterization of the teachings of Moller et al. nor of the rejection based thereon, Applicants note that each of claims 32, 38, 44, and 50 has been amended to recite a pharmaceutical composition comprising a somatostatin type-5 receptor selective agonist. Moller et al. neither teach nor suggest a composition comprising a somatostatin type-5 receptor selective agonist, much less that such a composition may be used to lower levels of lipids (claim 32), or of triacylglycerols (claim 38), or of glycerols (claim 44), or of cholesterol (claim 50). For the possible convenience of the Examiner, Applicants note that the term "somatostatin type-5 receptor selective agonist" is defined in the specification of the Instant Application as denoting "a somatostatin agonist which (1) has a higher binding affinity (i.e., Ki) for SSTR-5 than for either SSTR-1, SSTR-2, SSTR-3, or SSTR-4 and (2) decreases lipid levels (e.g., cholesterol, glycerols, or triacylglycerols) in a patient (e.g., as shown by the biological assay described [later in the specification]"; (Instant Application at page 9, lines 18 - 25). Indeed, not only is the somatostatin analog utilized by Moller et al. not an SSTR-*5* selective analog, (see Table II at p. 17 of WO 96/35950, which clearly teaches that SMS 201-995 is an SSTR-*2* selective analog), Moller explicitly teaches that SMS 201-995 had ***no effect*** on observed cholesterol levels. (See Moller et al. at p. 347, second column text.)

Applicants respectfully submit that the foregoing demonstrates that Moller et al. do not anticipate the claims of the Instant Application as currently amended. Accordingly, the rejection of claims 32, 38, 44 and 50 under 35 USC 102(b) as being anticipated by Moller et al., is obviated, and Applicants respectfully request withdrawal thereof

Rejections under 35 USC §103(a)

In the Instant Office Action the Examiner has rejected claims 1, 6, 8, 18, and 32-55 under 35 USC 103(a) as being unpatentable over Moller et al. (Clin. Science, vol. 75, pp. 345-350, 1998) taken with WO 96/35950 or Degrado. Applicants respectfully

traverse this rejection, both as put forth in the Instant Office Action at pages 5-6 and at pages 9 - 11.

Applicants have cancelled claims 1, 6, 8, 18, 33, 36-37, 39, 42-43, 45, 48-49, 51, and 54-55 by the amendments submitted herewith. Accordingly, the rejection of claims 1, 6, 8, 18, 33, 36-37, 39, 42-43, 45, 48-49, 51, and 54-55 under 35 USC 103(a) as being unpatentable over Moller et al. taken with WO 96/35950 or Degrado is obviated, and Applicants respectfully request withdrawal thereof.

Regarding claims 32, 34-35, 38, 40-41, 44, 46-47, 50 and 52-53, without conceding the correctness of the Examiner's characterization of the teachings of Moller et al., WO 96/35950 or of Degrado, nor of the rejection based thereon, Applicants have amended claims 32, 38, 44 and 50 such that these claims are now drawn to a pharmaceutical composition comprising a somatostatin type-5 receptor selective agonist.

Neither Moller et al., nor WO 96/35950 nor Degrado, either alone or in combination, teach or suggest a composition comprising a somatostatin type-5 receptor selective agonist, much less that such a composition may be used to lower levels of lipids (claims 32, 34 and 35), or of triacylglycerols (claims 38, 40 and 41), or of glycerols (claims 44, 46 and 47), or of cholesterol (claims 50, 52 and 53).

Further, as noted above WO 96/35950 teaches that SMS 201-995 is a somatostatin type-*2* receptor selective agonist, not a somatostatin type-*5* receptor selective agonist. Thus neither Moller et al. nor WO 96/35950, either alone or combination, either teach or suggest the use of somatostatin type-5 receptor selective agonists for any purpose, much less that somatostatin type-5 receptor selective agonists would be useful for treating hyperlipidemia.

Further still, Degrado provides no useful information whatsoever in respect of providing compounds for the treatment of hyperlipidemia. Rather Degrado merely states, in general terms, that D-amino acids may be incorporated into peptides with the hope of achieving greater stability. Degrado provides no direction regarding in which peptides, among the millions of possible candidates, one or more D-amino acid substitutions may be made, much less any guidance as to which position(s) within any such peptide D-amino acid substitutions should be make, much less still which specific D-amino acids should be utilized. Significantly, Degrado itself teaches that D-amino acid substitution

does not necessarily produce active peptides: "the resulting analogs, ***if active,*** would have enhanced stabilities to enzymatic degradation" (emphasis added). (Degrado at page 60, lines 4-5.) The necessary implication is that it is unknown at the outset whether a peptide will retain activity once a D-amino acid has been incorporated therein.

Applicants respectfully submit that the foregoing demonstrates that neither Moller et al., nor WO96/05950, nor Degrado, either alone or in combination, teach all the elements of the claims of the Instant Application as currently amended. Accordingly, the rejection of claims 32-55 under 35 USC 103(a) as being unpatentable over Moller et al. in combination with WO 96/35950 or Degrado is obviated, and Applicants respectfully request withdrawal thereof

Rejection of Obviousness-Type Double Patenting

In the Instant Office Action the Examiner has rejected claims 1, 6, 8, 18 and 32-55 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-23 of U.S. Patent No. 6,004,928. Applicants respectfully traverse this rejection.

Applicants have cancelled claims 1, 6, 8, 18, 33, 36-37, 39, 42-43, 45, 48-49, 51, and 54-55 by the amendments submitted herewith. Accordingly, the rejection of claims 1, 6, 8, 18, 33, 36-37, 39, 42-43, 45, 48-49, 51, and 54-55 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-23 of U.S. Patent No 6,004,928 is obviated, and Applicants respectfully request withdrawal thereof.

Regarding claims 32, 34, 35, 38, 40, 41, 44, 46, 47, 50, 52 and 53, Applicants note that each of these claims is drawn to a pharmaceutical composition whereas each of the claims of U.S. Patent No. 6,004,928 is drawn to a method of treatment. Applicants direct the Examiner's attention to MPEP §806.05(h), which provides that claims may be pursued in separate patent applications if, *inter alia*, a process of using a product as claimed can be practiced with another materially different product. Applicants note that the process of treating, e.g., elevated cholesterol may be practiced by non-somatostatin compounds. For example, atorvastatin, (the synthetic compound which is the active

ingredient in LIPITOR), acts to reduce cholesterol by inhibiting 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase. b

Accordingly, the rejection of claims 32, 34, 35, 38, 40, 41, 44, 46, 47, 50, 52 and 53 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-23 of U.S. Patent No 6,004,928 is obviated, and Applicants respectfully request withdrawal thereof. However, if the Examiner considers that this rejection should be maintained, Applicants respectfully request that the rejection be held in abeyance until such time as an allowable set of claims has been achieved.

Conclusion

Based upon the foregoing Applicants respectfully submit that the pending claims, as presently amended, are in condition for allowance and notification to that effect is earnestly solicited. Examiner Mohamed is invited to telephone Applicant(s) attorney at (508) 478-0144 to facilitate prosecution of this application.

Respectfully submitted,

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